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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,649	07/01/2003	Chris Rundfeldt	HUBR-1221	2085

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EXAMINER	
KANTAMNENI, SHOBHA	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
06/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/611,649	RUNDFELDT ET AL.	
	Examiner	Art Unit	
	Shobha Kantamneni	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8-13,15,17,18 and 20-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *NONE* is/are allowed.

6)☒ Claim(s) *1-4, 6, 8-13, 15, 17-18, 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/04/2008 has been entered.

Applicant's amendment filed on 10/22/2007, wherein claims 1, and 20 have been amended.

Applicant's amendment overcomes the rejection of claim 20 under 35 U.S.C. 112, first paragraph.

Applicant's amendment overcomes the rejection of claims 1-4, 6, 8-13, 15, 17-18, 22 under 35 U.S.C. 102(b) as being anticipated by Ehinger et al. (NAUNYN-SCHMIEDEBERG'S ARCHIVES OF PHARMACOLOGY, vol. 363, no.4 Supplement, 2001, page R85, XP009019486 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology; Mainz, Germany; March 13-15, 2001, PTO-1449).

Claims 1-4, 6, 8-13, 15, 17-18, 20-23 are examined herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitations, "sympathomimetic amine, xanthine derivative, and adrenal stimulant" in claim 20, render claim 20 herein indefinite. The recitations, "sympathomimetic amine, xanthine derivative, and adrenal stimulant" are not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to what compounds are encompassed by the recitations "sympathomimetic amine, xanthine derivative, and adrenal stimulant" herein. For example, one of ordinary skill in the art would clearly recognize that many widely varying groups could possibly substituting the xanthine herein would read on the "derivative" of xanthine.

Given the fact that any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. It is unclear and indefinite as to the compounds encompassed by the recitations "sympathomimetic amine, xanthine derivative, and adrenal stimulant" herein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 8-13, 15, 17-18, 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ehinger et al. (NAUNYN-SCHMIEDEBERG'S ARCHIVES OF PHARMACOLOGY, vol. 363, no.4 Supplement, 2001, page R85, XP009019486 42nd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology; Mainz, Germany; March 13-15, 2001, PTO-1449).

Ehinger et al. disclose the employment of AWD 12281 ((N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide) to treat atopic dermatitis. Experiments with toluene-2,4-diisocyanate (TDI)-sensitized mice was disclosed. TDI challenged mice were treated by topically applying AWD 12281 (0.1-3 %) i.e after an allergic challenge. Ehinger et al. discloses the use of AWD 12281 to treat atopic dermatitis. In some of the experiments with TDI-sensitized mice, the AWD was applied topically once or thrice in 24 hours. See the entire paper.

Ehinger et al. do not explicitly teach that (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is administered to mice for the first time after an allergic challenge.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the first time after an allergic challenge with reasonable expectation of treating atopic dermatitis because according to Ehinger et al. (N-3,5-

dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is known to treat allergic skin diseases such as atopic dermatitis.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide up to 48 h after an allergic challenge.

One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen i.e administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the first time after an allergic challenge, and to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide up to 48 h after an allergic challenge because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in pharmaceutical art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-21, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ehinger et al. as applied to claims 1-4, 6, 8-13, 15, 17-18, and 22 above, in view of Winger (US 5,767,095, PTO-892).

Ehinger et al. is as discussed above.

Ehinger et al. does not teach the employment of a pharmaceutical agent, corticosteroid in combination with AWD 12281 in the method of treating atopic dermatitis.

Winger teaches that corticosterioids are known for the treatment of canine atopic dermatitis. See column 25, lines 19-22.

It is generally considered *prima facia* obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. As shown by recited teachings of Ehinger and Winger the instant claims contain two compounds used for treatment of skin condition such as atopic dermatitis. *In re Kerkohoven*, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 8-13, 15, 17-18, 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baumer et al. (European Journal of Pharmacology, 446, 2002, pages 195-200, PTO-1449).

Baumer et al. disclose the employment of AWD 12-281 ((N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide) to treat allergic dermatitis in mice. To obtain an allergic dermatitis, BALB/c mice were sensitized to toluene-2,4-diisocyanate (TDI). TDI challenged mice were treated by topically applying AWD 12281 (0.1-3 %). It is disclosed that AWD 12-281 inhibited the ear swelling significantly 8, 16, 24, and 48 h. See abstract; page 196, right-hand column, paragraph 2-page 197, right-hand column, paragraph 1; page 198, left-hand column, last paragraph-page 199, paragraph 1.

Baumer et al. do not explicitly teach that (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is administered to mice for the first time after an allergic challenge.

Baumer et al. do not explicitly teach that (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is administered to mice up to 48 h after an allergic challenge.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the first time after an allergic challenge with reasonable

expectation of treating atopic dermatitis because according to Baumer et al. (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is known to treat allergic skin diseases such as allergic dermatitis.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide up to 48 h after an allergic challenge.

One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen i.e administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide after an allergic challenge, and to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide up to 48 h after an allergic challenge because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in pharmaceutical art.

Response to Arguments

Applicant argues that "the Examiner is invited to review the claims because according to the pending claims first AWD12-281 administration takes place after the allergic challenge and, the success of this method was not obvious as similar experiments here the PDE4 inhibitor cilomilast was administered after TDI challenge failed to be effective." These arguments have been considered, but not found persuasive because the arguments are not in commensurate in scope with the instant claims. The instant method is drawn to employing AWD 12-281 in treating allergic skin disease, and not to employing a PDE4 inhibitor. It is pointed out that it is irrelevant if

PDE4 inhibitor, cilomilast works in the method herein, since the structure of cilomilast is very different from the AWD 12-281 employed in the method herein.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the first time after an allergic challenge with reasonable expectation of treating atopic dermatitis because 1) according to Baumer et al. (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is known to treat allergic skin diseases such as allergic dermatitis, and further 2) the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in pharmaceutical art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 8-13, 15, 17-18, 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hofgen et al. (US 6, 251, 923, PTO-1449).

Hofgen et al. discloses hydroxyindoles of the Formula (I), including the instantly elected species (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the treatment of skin diseases such as psoriasis, keratosis,

atopic dermatitis (allergic dermatitis), eczema. See abstract; column 7, lines 25-34; column 10, EXAMPLE 1. Oily suspensions for topical application comprising other agents such as fatty acid esters is also taught. See column 8, lines 43-45.

Hofgen et al. do not explicitly teach that (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is administered for the first time after an allergic challenge.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the first time after an allergic challenge with reasonable expectation of treating atopic dermatitis because according to Hofgen et al. (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide is known to treat allergic skin diseases such as atopic dermatitis, eczema.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide up to 48 h after an allergic challenge.

One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen i.e administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide after an allergic challenge, and to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide up to 48 h after an allergic challenge because the optimization of result

effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in pharmaceutical art.

Response to Arguments

Applicant argues that "Hofgen does not specifically disclose the treatment of allergic skin diseases in which the medicament is topically administered after an allergic challenge." These arguments have been considered, but not found persuasive.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the first time after an allergic challenge with reasonable expectation of treating atopic dermatitis because 1) Hofgen et al. discloses topical administration of hydroxyindoles of the Formula (I), including the instantly elected species (N-3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide for the treatment of skin diseases such as psoriasis, keratosis, atopic dermatitis (allergic dermatitis), and further 2) the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in pharmaceutical art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6, 8-13, 17-18, are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-29, 36-38, and 69-84 of co-pending Application No. 10/856034. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of treating skin disease comprising topically administering N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide, and '034 is drawn to a method of treating atopic dermatitis comprising administering a compound, N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide. The application '034 does not specifically teach the topical administration of the compound in the method therein. It would have been obvious to the person of ordinary skill in the art at the time of invention to administer topically to a subject a therapeutically effective amount of N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3yl]-2-oxoacetamide with reasonable expectation of treating a skin disorder. Further, topical administration of compounds is well known for

treating skin disorders, and '034 discloses that the compounds therein can be administered topically. See page 14 of '034.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to applicant's argument: Applicant's arguments have been considered, but not found persuasive as discussed above.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Tuesday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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